FRESENIUS KABI

OVER THE COUNTER (OTC) MEDICINES BUSINESS PROCESS REFORMS

Submission in Response to the TGA Consultation Paper, Version 1.0 September 2012

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TABLE OF CONTENTS

1. EXECUTIVE SUMMARY

The Therapeutic Goods Administration (TGA) has proposed reforms to the business process for Over the Counter (OTC) Medicines and requested input from industry regarding these reforms.

The key proposals of the TGA reforms include:

- A risk categorisation framework for new OTC medicine applications and applications to relating to changed medicines
- A revised OTC medicines evaluation process
- The development of OTC medicine monographs for well-characterised active ingredients
- Application categorisation for umbrella branded medicines
- The establishment of target timelines

Fresenius Kabi Australia (FKA) welcomes the opportunity to comment on the proposed changes. We have noted and broadly support the proposals set out and have only minor concerns regarding the realisation of these reforms.

FKA strongly believes that any reforms should only be implemented with due consideration of the benefit to stakeholders and the impact of regulatory burden to manufacturers and sponsors.

2. INTRODUCTION

Fresenius Kabi is a global enterprise offering excellence in products and services. We pride ourselves on being customer focused, providing solutions to problems and maintaining a competitive edge through cost leadership. We at Fresenius Kabi Australia (FKA) are a leading supplier of infusion solutions and medical systems and are committed to innovation in both products and services.

FKA welcomes the opportunity to comment on the TGA's proposed reforms to Australian business processes for Over the Counter (OTC) Medicines. The proposals result from a harmonized approach to the regulation of OTCs in Australia and New Zealand and are in the context of a three-stage approach to achieving the establishment of the Australia New Zealand Therapeutic Products Agency (ANTZPA) by 2016.

While FKA supports initiatives to increase the efficiency and transparency of the OTC evaluation process, direct comment on the TGA's specific proposals have been individually outlined in subsequent sections.

3. THE TGA PROPOSALS

The TGA proposals fall into five broad areas:

- Application of risk categorisation framework for new OTC medicine applications and applications to relating to changed medicines
- A revised OTC medicines evaluation process
- The development of OTC medicine monographs for well-characterised active ingredients
- Application categorisation for umbrella branded medicines
- The establishment of target timelines

The following comments are provided in response to each of the specific proposals.

3.1. RISK CATEGORISATION FRAMEWORK

3.1.1 TGA Proposal Summary

It is proposed that there would be five risk categories (Category N1 to Category N5) for applications for new medicines and four risk categories (Category C1 to Category C4) for applications relating to changed medicines.

Each application category will have clearly defined submission requirements and timelines. OTC medicines containing well-understood active ingredients and clones of existing OTC medicines would fall into the lower risk categories, while more complex applications such as those involving new active ingredients or new indications would fall into the higher risk categories.

Category 1 applications (N1 or C1) would require less supporting information and follow a shorter timeline than applications in higher categories (such as N5 or C4).

3.1.2 FKA Response to General Questions

a) Do you support the concept of risk-based categories for OTC medicines?

Improvements in business processes are an important part of improving, not only the efficiency of the submission process, but also the public's confidence in over the counter medicines. FKA recognises that in order to obtain such improvements, a multi-faceted approach is required including improvements in the approach to pre-market review through the use of risk profiles. As such the concept of risk-based categories for OTC medicines is supported.

b) Do you agree with the proposed risk categories for new medicines?

FKA broadly supports the proposed risk-based categorisation of new medicine applications.

c) Do you agree with the proposed risk categories for changed medicines?

FKA broadly supports the proposed risk-based categorisation for changed medicine applications. However, it is noted that there is no mention of changes for which there is currently no requirement for TGA notification. The current ARGOM contains reference to such changes in the Changes Table as status code *O* (i.e. primary packaging specification changes, code KPP). While it understood that one of the main purposes of this consultation is to outline requirements for those changes requiring submissions/notifications, it is of import to clarify whether the reform will consequently impact those changes currently not requiring notification.

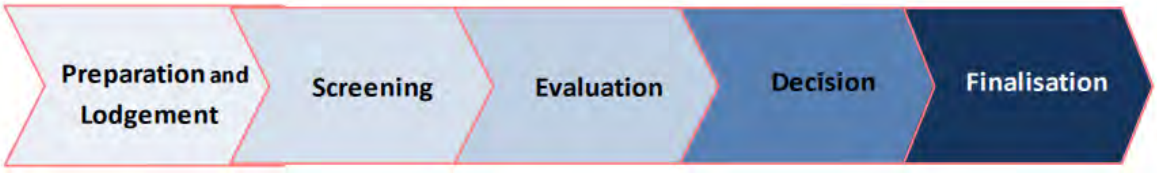
3.1.3 Other FKA Comments

It is also appreciated that part of the impetus driving these business process reforms is the need to move away from a 'page-count' framework of assessment to a structure based on risk categorisation. However, whilst supporting the proposed categories, FKA believes it is important to highlight the lack of guidance on issues relating to grandfathered OTC products. Many grandfathered products may have been entered on the ARTG with limited assessment and with incomplete details on the register. Such products appear to fall within a grey area of assessment when changes or updates are required. As such, clarification regarding how such products will be addressed in the current reforms is sought.

3.2. OTC MEDICINES EVALUATION PROCESS

3.2.1 TGA Proposal Summary

The proposed process is made up of five phases each with defined requirements for progressing to the next phase.



The following principles have been applied in developing the proposed process.

a) Applications will be screened by the regulator upon receipt.
b) Incomplete applications will not be accepted for evaluation and fees will be forfeited.
c) There will be a maximum of two rounds of requests from the regulator for the applicant to supply additional information.
d) Target timelines will be specified for the completion of each stage of the evaluation process.
e) Target timelines will be specified for receipt of company responses to requests for additional information.
f) The regulators will report actual time taken to complete stages in the evaluation process.
g) Applicants will be able to monitor progress of applications through online access to a database maintained by the regulator

3.2.2 FKA Response to General Questions

a) Do you support the proposed five-phase process?

FKA broadly supports the five-phase process that is proposed.

The screening phase is noted as having two parts (the first being an administrative check, with the second being a technical screen). This phase should, theoretically, eliminate any applications that are obviously lacking. However, there is concern regarding those applications that have passed satisfactorily through this phase but may have deficiencies only recognised during the evaluation phase. It is anticipated that the sponsors of such applications would be provided the opportunity to address these deficiencies without the applications being deemed ineffective. Such requests to address deficiencies overlooked in the screening phase should also not be considered as part of the two rounds of Requests for Information (RFI).

The decision phase under the joint regulatory scheme is also noted as being a single decision-making process with effect in both countries. However, until ANZTPA is established, the decision-making process will remain as it is currently. However, no details of what transitional arrangement will be provided in those applications where there are discrepancies/differences between the decisions made by the TGA and Medsafe. Such details are of importance for those sponsors who currently supply the same product in both Australia and New Zealand.

b) Do you agree with the principles that were applied when developing the proposed process?

The proposed streamlined submission process is based on a series of milestones, the underlying principles of which are similar to those already underpinning the business process for prescription medicines. These principles are recognised as a means of improving the transparent of the overall submission process, as well improving the quality of submissions received by the TGA. As such, there is no objection by FKA.

3.2.3 Other FKA Comments

Improvements in business processes (including evidence requirements) are an important part of improving, not only the efficiency of the submission process, but also the public's confidence in over the counter medicines. While FKA agrees with these principles, it is important to highlight the experience of the prescription business process reforms. In the latest *TGA Prescription Medicines* Streamlined *Submissions Process Newsletter* (June 2012) it was noted that the TGA was not able to consistently meet several milestone dates. This result was, in part, attributed to resource challenges posed by dual application processing (under the old and new processes). In learning from this experience, the issue of TGA resources during the transition period for OTC applications is of great concern for FKA. Such resource challenges should be duly considered in the implementation of these reforms.

In the implementation of these reforms, the issue of TGA flexibility in relation to application acceptance need also be considered. It is understood that it ultimately the sponsor's responsibility to ensure that applications are complete and are in-line with TGA requirements. However, given the TGA's previous approach to OTC medicine submissions, it must be said that Industry has historically benefited from a degree of flexibility in the TGA's acceptance of applications of varying quality. While this variation is submission quality is indeed a driving force for these reforms, Industry should not be unfairly burdened with an expectation to convert to the new process without due consideration from the TGA. In particular, the screening phase, while recognised as being useful tool to eliminate those applications that are clearly deficient, should not be implemented as simply a 'box-ticking' exercise. As was experienced with the transition period for the prescription medicine business process reforms, a similar period of change-over should be applied to the OTC medicine reforms. In particular, the 48 hour 'grace period' that was permitted for the prescription reforms (enabling sponsors to rectify deficiencies in submission dossiers) proved a welcome compromise that enabled sponsors to address deficiencies that may have been overlooked in error. As with the prescription reforms, this grace period would only be a temporary measure to smooth the transition from the new to the old process.

3.3. OTC MEDICINE MONOGRAPHS

3.3.1 TGA Proposal Summary

It is proposed that OTC medicine monographs (OMMs) will be developed for OTC medicines containing well-characterised active ingredients. The monographs will specify requirements in relation to:

a) active ingredients, dosage forms and strengths
b) indications and claims
c) directions for use
d) labelling and advisory statements
e) quality standards

3.3.2 FKA Response to General Questions

a) Do you support the concept of developing monographs for some OTC medicines?

FKA supports the concept of developing specific monographs for OTC medicines. The existence of OTC monographs would enhance the understanding of the specific requirements for various well-characterised active ingredients. The ability to leverage compliance with an OMM in the submission of abbreviated data packages also poses a distinct advantage.

b) Do you agree with the proposed list of medicines that should be given priority for monograph development?

FKA agrees with the proposed list of medicines selected for priority OMM development.

3.3.3 Other FKA Comments

It is appreciated that several active ingredients, based on analysis of recent Australian applications, have been selected as priority targets for the development of OMMs, while OMMs will be developed at a later date for other active ingredients. However, details of how these additional targets for OMMs will be selected and the ranking of priority applied have not been provided. Details regarding the proposed frequency of the reviews required for identifying additional OMM targets have also not been supplied.

In parallel to the TGA's selection of ingredients for targeted OMMs, the ability for a manufacturer to nominate particular active ingredients for the development of an OMM should also be considered. Such nominations would of course require support by a detailed argument for acceptance by the TGA.

Following the issuance of an OMM, a system of review will be required to maintain currency and to address concerns/issues as they arise. However, no details regarding the frequency of such reviews have been provided. In the instance that

a monograph is updated following a review, information regarding the timeframe permitted for a manufacturer to incorporate the changes to maintain compliance and the level of assessment required should also be provided.

For those manufacturers opting for compliance with an OMM, abbreviated reviews are a distinct advantage. This advantage is off-set by post-market monitoring for compliance. While post-market surveillance is already applied to OTC medicines, it is not clear whether there will be a targeted approach to those products for which compliance to an OMM is claimed. In particular, it is important to understand whether there will be an increase in post-market monitoring of these products as a consequence of reduced pre-market assessment.

Lastly, while compliance to an OMM is recognised as a distinct advantage, this compliance should not be made mandatory. Rather, OMMs should be viewed as a favourable means to establish compliance for their respective active ingredients.

3.4. UMBRELLA BRANDED MEDICINE

3.4.1 TGA Proposal Summary

Determination of the application category for an umbrella branded product should be made using the criteria set out in the proposed risk categorisation frameworks.

Within the proposed risk categorisation frameworks, applications for umbrella brand extensions are identified as requiring an increased level of assessment when the risks to consumers are considered to be higher. These applications are classified as category N4 or N5 for new medicines and category C3 or C4 for changed medicines. Medsafe and the TGA will develop guidelines, based on the following approach, to assist sponsors to determine the correct application risk category for applications relating to an umbrella branded medicine.

3.4.2 FKA Response

FKA supports the general principles outlined in this proposal.

3.5. TARGET TIMELIMES

3.5.1 TGA Proposal

The target timelines proposed for the joint regulatory scheme are shorter than those currently achieved by either Medsafe or the TGA.

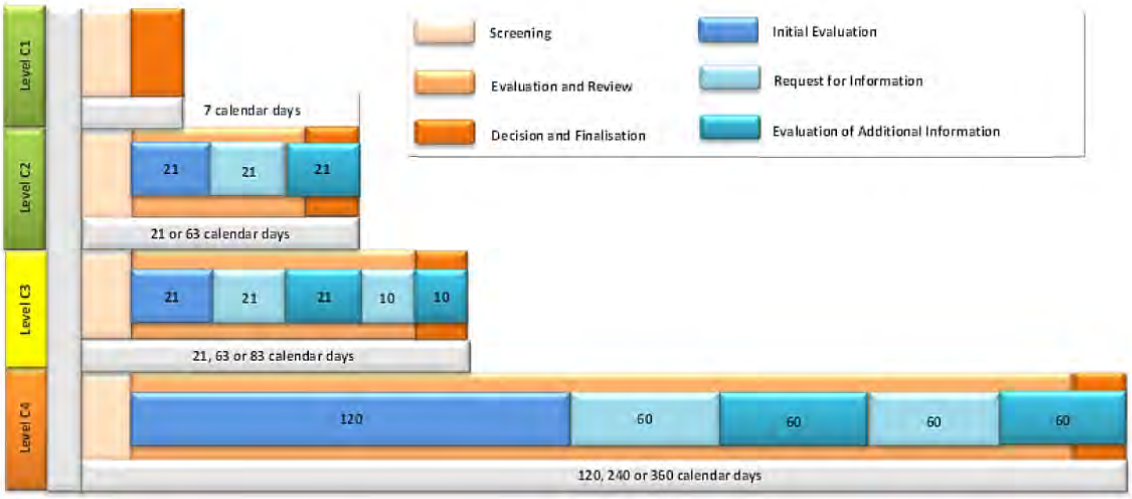


Figure 6: Aspirational timelines for changed medicine applications

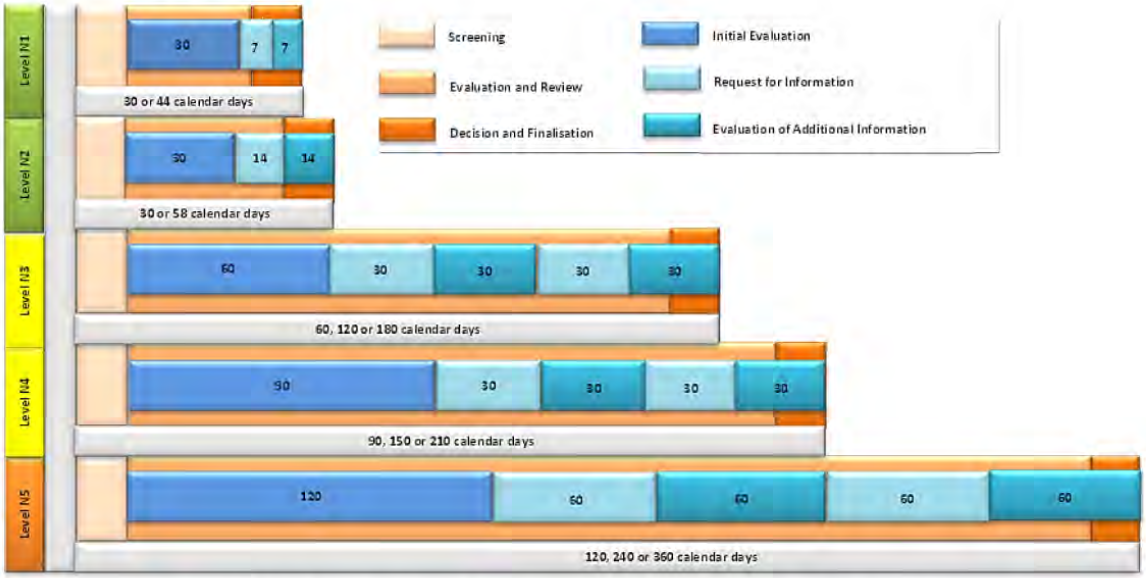


Figure 5: Aspirational timelines for new medicine applications

3.5.2 FKA Response

The proposed timelines are a desirable move away from the current practice in which applications subject to a 'queuing time'. However, in learning from the experiences of the prescription business process reforms, it was recognised that the TGA may not be meeting the required milestones. While such delays may be beyond the control of the TGA and the sponsor in some cases, where the delay is not attributed to the sponsor, the consequences of non-compliance to a milestone should be identified. Currently, section 24D of the *Therapeutic Goods Act 1989* states that, were whole fee has been paid and the evaluation is not completed within the specified period, then 25% of the fee must be refunded. However, as the proposed paper refers to 'aspiration' timeframes, it is not clear whether section

of the Act can be applied to these timeframes prior to the establishment of ANTZPA in 2016.